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May 4, 2000

CERTIFIED MAIL –
RETURN RECEIPT REQUESTED

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Park Building, Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

Re: Docket No. 99P-4053/CP 1
Citizen's Petition re: Proposed Amendment to Classification and Product Labeling for the Sympathominetic [sic] Amine Phentermine

Dear Ladies and Gentlemen:

This firm is counsel to Medeva Pharmaceuticals, Inc. and Medeva Pharmaceuticals Manufacturing, Inc. ("Medeva") in connection with various pending litigations arising out of the use of the anorectic agents fenfluramine, dexfenfluramine and phentermine. Medeva is the manufacturer of Ionamin® (phentermine resin) capsules C-IV. Among the actions in which we represent Medeva is the Multidistrict Litigation proceeding entitled *In re Diet Drugs Products Liability Litigation* (MDL No. 1203), pending before Hon. Louis C. Bechtle in the United States District Court for the Eastern District of Pennsylvania (the "MDL").

We have reviewed a copy of the March 4, 2000 letter to docket No. 99P-4053/CP1 from Timothy J. Maher, Ph.D. and Richard J. Wurtman, M.D. in support of the above-referenced Citizen's Petition.

99P-4053

C3

Medeva does not believe that anything set forth in the March 4 letter from Drs. Wurtman and Maher supports the Petition in any way or requires a lengthy response. Medeva believes that its position is adequately set forth in the November 4, 1999 submission to the docket from Dr. Terrance C. Coyne, Medeva's Vice President of Medical, Scientific and Legal Affairs, and in this firm's submission of November 15, 1999. Although Medeva disagrees with most of the comments in the March 4 letter, these disagreements do not affect the conclusion that the Petition is without merit.

The comments contained in the March 4 letter from Drs. Wurtman and Maher fail to address Medeva's central criticism of their Petition. Specifically, Drs. Wurtman and Maher continue to insist that phentermine is a MAOI without indicating or even addressing the concentration necessary in humans to produce this effect. Indeed, they do not refer to any quantitative data whatsoever (*i.e.*, the clinical blood plasma levels of phentermine or the concentration of phentermine necessary to produce a MAO inhibitory effect) in their original Petition or in their March 4 letter intended to "rebut" Medeva's criticisms. It is a well-accepted tenet of pharmacology that at high enough concentrations, any compound is capable of producing certain effects in the body. To scientifically assess whether a substance is a MAOI, the concentration of that substance required to inhibit MAO must be compared to the clinical blood plasma levels of the substance. By ignoring this quantitative data concerning phentermine, Drs. Wurtman and Maher fail to address the key reason why phentermine – administered at clinical doses in humans – is not a MAOI.

The FDA should be aware that at the recent *Daubert* hearing held in the MDL proceeding referred to above, the phentermine manufacturers challenged the scientific reliability of the opinion testimony of plaintiffs' experts Dr. Maher and Paul Wellman, Ph.D. At the hearing, plaintiffs (and Dr. Maher, in particular) endeavored to bolster the reliability of their opinions by reference to the fact that a Citizen's Petition had been filed with the FDA. (*See, e.g.*, MDL *Daubert* Hearing Transcript, March 7, 2000, at pp. 65-66, attached hereto as Exhibit A.) We believe that using the Citizen's Petition process to further litigation goals is inappropriate.

Respectfully submitted,

David M. Cohen

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

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IN RE: DIET DRUGS (Phentermine/:
Fenfluramine/Dexfenfluramine : MDL DOCKET NO. 1203
PRODUCTS LIABILITY LITIGATION : ALL CASES

Philadelphia, Pa.
March 7, 2000

BEFORE LOUIS C. BECHTLE, CH. J. EMERITUS

DAUBERT HEARING

APPEARANCES:

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an in vitro assay, we could inhibit MAO as had been published in the literature.

That both of those results, the human and the rat study are combined in the Lancet article, which was published in January of '99.

Q. Okay.

The next slide is 22?

A. This slide is labeled, titled Failure To Label Phentermine As A Monoamine Oxidase Inhibitor.

Q. Are some drugs so labeled?

A. Yes. There are some drugs recognized by all as being monoamine oxidase inhibitors.

Q. Phentermine was not so labeled, is that correct?

A. Phentermine was not, despite the fact that the literature indicated that it was capable of inhibiting this enzyme monoamine oxidase.

The connection with Pondimin is that the PDR and other documents indicate that Pondimin should not be used with a monoamine oxidase inhibitor within two weeks of discontinuance of the MAOI.

Now, had phentermine been labeled as a monoamine oxidase inhibitor, I believe no responsible physician would have ever prescribed phentermine with any of the fenfluramines, and I

believe this to the point that myself and Dr. Wurtman have petitioned the FDA requesting that they consider relabeling phentermine as a monoamine oxidase inhibitor, so as to prevent the use of other seratonin reuptake inhibitors with phentermine.

Q. Is that petition now actively pending before the FDA?

A. Yes. We submitted that some time ago and we recently submitted an update, which was really a response to, I believe, the phentermine manufacturers criticisms of our petition.

Q. The phentermine manufacturers have responded to the petition. Then Dr. Wurtman, Dr. Maher have recently filed a reply. All of that process is going on, this is not a surprise to the other side. They are participating in that struggle with the FDA as well.

The next slide, please.

Now we are switching from primary pulmonary hypertension.

THE COURT: It is 23.

BY MR. WILLIAMS:

Q. We are switching now, your Honor, from PPH, the pulmonary hypertension disease caused by fenfluramine to valvular heart disease.

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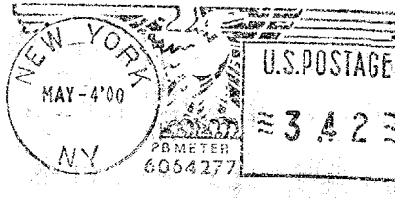

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